

May 29, 2003

Richard Henrich
Manager, Regulatory Affairs
Great Lakes Chemical Corporation
Highway 52, N.W.
West Lafayette, IN 47996

Dear Mr. Henrich:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2,4,6,-Tribromophenol posted on the ChemRTK HPV Challenge Program Web site on January 24, 2003. I commend Great Lakes Chemical Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Great Lakes Chemical Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission: 2,4,6-Tribromophenol

Summary of EPA Comments

The sponsor, Great Lakes Chemical Corporation, submitted a test plan and robust summaries to EPA for 2,4,6-tribromophenol (TBP, CAS No. 118-79-6) dated December 27, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 24, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The data provided by the submitter for melting point, boiling point, and partition coefficient are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured data for vapor pressure and resolve the discrepancy between the water solubility values provided.
2. Environmental Fate. (a) The data provided by the submitter for biodegradation are adequate for the purposes of the HPV Challenge Program. (b) Even though the test plan indicates that this chemical will not hydrolyze, the submitter needs to incorporate this information in the robust summary. (c) The submitter needs to provide data for the reaction of this chemical with photochemically generated hydroxyl radicals, and for transport and distribution (fugacity).
3. Health Effects. Data for acute toxicity and chromosomal aberration endpoints are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of the gene mutation assay (Ames test) pending submission of additional information. Submitted data for repeated-dose toxicity and reproductive and developmental toxicity are inadequate and testing is needed for these endpoints.
4. Ecological Effects. The data for fish and invertebrates endpoints are adequate, but the submitter needs to provide the missing study details. EPA agrees with the submitter's plan to perform a test for toxicity to algae.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the 2,4,6-tribromophenol Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

The data provided by the submitter for melting point, boiling point, and partition coefficient are adequate for the purposes of the HPV Challenge Program.

Vapor pressure. The submitter provided an estimated vapor pressure value of 5.72×10^{-5} mm Hg at 25 °C. According to OECD guidelines, calculations showing a value less than 1×10^{-5} Pa (8×10^{-8} mm Hg) at 25 °C may be acceptable in lieu of measuring vapor pressure. Since the estimate is greater than 8×10^{-8} mm Hg at 25 °C, the submitter needs to provide measured data for this endpoint.

Water Solubility. The water solubility values provided by the submitter are substantially different from each other (70 mg/l vs. 996 mg/l). The submitter needs to resolve the discrepancy between these values, or provide measured water solubility data following OECD guidelines.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The data provided by the submitter for biodegradation are adequate for the purposes of the HPV Challenge Program.

It is unclear why the sponsor twice uses the phrase “hydrocarbon components of substances in this chemical group” to refer to (apparently) the title substance.

Stability in water. The submitter needs to refer its explanation specifically to TBP (not “hydrocarbons”) and to include the information in the in the robust summaries.

Photodegradation. The submitter needs to include data for the reaction of this chemical with photochemically generated hydroxyl radicals. The submitter’s extrapolation from data on volatilized hydrocarbons is not adequate. An estimated value using the AOPWIN model would satisfy the endpoint. The measured solid phase and aqueous phase direct photolysis data provided by the submitter are adequate.

Transport and distribution (fugacity). In the test plan, the submitter states that adequate data exist for similar compounds and that compounds with higher molecular weights in this group will partition mostly to soil, but did not provide a robust summary. The submitter needs to provide transport and distribution data for TBP. Although EPA had previously recommended the use of the level I model, this model is somewhat limited. EPA now recommends the use of the level III model, which is more useful for estimating a chemical’s fate in the environment on a regional basis. When developing its model, the submitter needs to incorporate in its robust summary the input values used in the estimation process.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

The submitted data for acute toxicity and the genetic endpoint for chromosomal aberrations are adequate for the purposes of the HPV Program.

Genetic toxicity. EPA reserves judgement on the adequacy of the gene mutation assay (Ames test) pending submission of additional information.

Repeated-Dose Toxicity. The submitted data do not adequately address the endpoint for repeated-dose toxicity. The information in the Hazardous Substances Data Bank indicates that the test material is highly, acutely toxic to humans exposed dermally or via inhalation. However, the submitted data did not show any significant toxicity in the 21-day inhalation study (an inadequate exposure period) in rats or the 28-day dermal study in rabbits. In addition, both summaries lack important details and, in the inhalation study, two dose levels rather than three were used. The NIOSH monitoring data¹ indicate that the general population may be exposed to this chemical via ingestion of food and drinking water. EPA believes that since exposure to the general population is by oral routes, and the existing data are judged inadequate, data from oral repeated-dose studies is needed. Therefore, EPA recommends that a combined repeated-dose/reproduction/developmental toxicity screening test (OECD 422) be conducted.

Reproductive/Developmental Toxicity. No reproduction toxicity data are available (no data on the reproductive organs from the repeated-dose studies are presented and, in any event, the exposure durations were shorter than the 90-day minimum to accept such data from repeated-dose toxicity studies). The submitted data do not provide sufficient details on the developmental effects of the chemical. EPA recommends a combined test (OECD 422) to assess these endpoints.

Ecological Effects (fish, invertebrates, and algae).

Fish and Invertebrates. The data for these endpoints are adequate, but the submitter needs to provide the missing study details.

Algae. EPA agrees with the submitter’s plan to perform a test for toxicity to algae. The study should be conducted according to OECD Guideline 201.

Specific Comments on the Robust Summaries

Generic comments

Information on the purity of the test substance was not included in most of the robust summaries for health effects.

Physicochemical Properties

Water solubility. The submitter indicates in its test plan that the water solubility of this chemical is 996 mg/L at 35 °C. However, in the robust summary, it indicates that the water solubility "at 15, 25, and 35 degrees °C, respectively were 996, 969 and 884". The submitter needs to address this discrepancy.

Health Effects

Genetic Toxicity. The submitter needs to provide additional information identifying the test strains and positive controls used in the Ames assay.

Repeated-Dose Toxicity. The 21-day inhalation study in rats (no date available) lacks the following information: particle size distribution; the type of exposure (e.g. whole body); whether feed consumption and specific hematological parameters were monitored; organ weight data; organs that were examined histopathologically; and type, incidence, and severity of lesions noted for kidney and liver.

The summary for the 28-day dermal study in rabbits did not include information on the skin surface area that was treated, whether feed consumption was monitored, which hematological and clinical chemistry parameters were assessed, which organs were weighed at necropsy and which organs were examined for histopathology.

Developmental Toxicity. The summary of the International Research and Development Corp. study lacked specific details such as the developmental parameters examined and the statistical treatment of the data from individual animals or litters. The summary of a study by Lyubimov, using whole body exposures failed to include specific details on developmental parameters (e.g., number and type of skeletal and soft tissue anomalies observed, etc.) however, the focus of the study is neurotoxicity.

Ecological Effects

Fish and Invertebrates. Information missing from the robust summary of acute toxicity of TBP to fish and daphnia included test substance purity, number and specifications of organisms tested, concentrations tested, mortality and effects seen at each concentration, control use and response, and statistical methods used. The submitter needs to provide the missing information.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

References

¹ NIOSH; National Occupational Exposures Survey (NOES) (1983)